MYXŒDEMA.

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It is reasonable to suppose cases of this somewhat rare disease, now known as myxœdema, have from time to time come under the observation of earlier physicians, and have been regarded as cases of other diseases, such, perhaps, as cretinism, renal anasarca without albuminuria, polysarcia, or, possibly, sclerema or locomotor ataxy, with all of which myxœdema might have been confused. For the differentiation of the disease the profession have to thank Sir William Gull, who was the first to describe it as a distinct disease in a paper on a "Cretinoid Condition Supervening in Women in Adult Life," read before the Clinical Society of London in 1874. In addition to the five cases then described by Dr. Gull, Dr. William Ord, three years later, was able to describe five more before the Royal Medical and Chirurgical Society of London. Of the two of these which had died, one had been carefully examined post mortem, with interesting results. The nearly, if not quite, universal mucous œdema, having an apparently causal relation to the clinical phenomena, seemed to justify Dr. Ord in naming the disease myxœdema. Including the above cases, there have been, up to the present time, about thirty brought to the notice of the two societies, the other gentlemen to whom the societies are indebted being Drs. Sanders (of Edinburgh), Duckworth, Goodhart, Sémon, Hadden, Lloyd, Andrew Clark, and Greenhow.

In France, M. Charcot had independently discovered the same disease, and was about to publish a paper on the subject, under the title "Cachexie Pachydermie," when he became acquainted with the researches of Dr. Ord, and adopted Dr. Ord's nomenclature. In our own country, so far as I can discover, Dr. William A. Hammond, of New York, was the first to recognize a case of myxœdema; of this, "with special reference to its cerebral and nervous

symptoms," he gave a detailed account before the American Neurological Association in June of last year. Besides what has been published in Transactions of societies, little has appeared in print concerning myxœdema, the most important papers being a "Clinical Lecture on Myxœdema,* by William Ord, M.D., F.R.C.P., Physician to and Lecturer on Medicine at St. Thomas's Hospital" (London), "Du myxœdème,† par Hadden, D.M., membre de la Société Pathologique de Londres, et ancien 'Medical Registrar' de St. Thomas's Hospital," and Dr. Bristow's article in the second and third editions of his "Treatise on the Theory and Practice of Medicine."

The etiology of myxœdema is obscure. At first the disease was thought to be confined to adult women, and the few cases occurring in men, reported by Drs. Fernn, Savage, and Hadden, and M.M. Charcot and Olive, were regarded as exceptional until quite recently. At a meeting of the Clinical Society, January 14, 1881, Dr. Andrew Clark said, for ten years he had been more or less familiar with cases agreeing with those principally described by Drs. Ord and Duckworth, but that the majority of his cases had been in men. Most recorded cases, however, have been in women between the ages of thirty and sixty. The disease is not endemic, epidemic, or hereditary; is not syphilitic or a result of excess in eating or drinking. It is seen in both the single and married, and in those of light and dark complexion. It has followed acute rheumatism and pregnancies. In one instance (Dr. Sémon's case) it has occurred directly after an injury to the brain, and in another (Dr. Ord's case, very advanced) its course has been hastened to a fatal end by the receipt of bad news. Perhaps the most common event in previous histories is frequency

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* British Medical Journal, May 11, 1878.

† Progrès médical, 1880, Nos. 30 et 31. See also British Medical Journal, October 27, 1877, April 27, 1878, October 18, 1879, November 20 and 27, 1880, January 22, 1881; Lancet, October 27, 1877, April 27, 1878, October 18, 1879, November 20, 1880, January 22, 1881; Medical Press and Circular, October 15, 1879; Medical Times and Gazette, May 1, 1880; Journal de médecine et de chirurgie, July, 1879; American Journal of Medical Sciences, July, 1875, and April, 1879; New York Medical Record, September 20 and November 29, 1879, and August 28, 1880.

of labors and miscarriages, or some uterine irregularity. But it must be confessed, as is true of many another disease, that little is known about the causes of myxœdema, and that that little is negative rather than positive. It might be said of mucoid changes in general, and they are by no means common, the most frequently seen is peculiar to the cartilages of old age, suggesting myxœdema may perhaps in part be due to such various causes as greatly exhaust vitality, such as, for instance, "fourteen children and seven miscarriages," as occurred in Dr. Sémon's case.

Of the five fatal cases recorded (three, Dr. Ord's; one, Dr. Greenhow's; and one, Dr. Lloyd's) at least two have been, and one is being thoroughly examined for pathological changes. Dr. Ord finds the essential lesion to be in the connective tissue. Its fibrillar element is remarkably increased, and the fibrils separated by unusually large interstices filled with transparent material yielding mucin, an excess of the normal intercellular cement, together with ab-

FIG. 1.—Section of a small artery from the tongue. The lumen is filled with blood-corpuscles. The thickened middle coat with nuclei is surrounded by the adventitia, swollen, fibrillated, and with nuclei. A fat-cell is seen to the left. Magnified 200 diameters.

normally numerous swollen nuclei. The fibrils are unusually distinct, being swollen as well as teased apart, as it were, by the interfibrillar material. With the great overgrowth of the mucin cementing material, connective tissue appears embryonic, even resembling the umbilical cord, and suggests a retrograde metamorphosis. The skin, subjected to chemical examination, is found to contain as much as fifty times the scarcely weighable quantity found in

of mucin

ordinarily œdematous, or healthy, skin. A portion of skin cut from the body retains its shape, the œdema being somewhat solid, while dropsical skin under the same conditions collapses as the fluid oozes from it. The new material surrounds and partially insulates the touch-corpuscles and other nerve-terminations; surrounds and chokes the secretory glands; but is most abundant in the lymphatic spaces and the loose cellular tissue around the blood-vessels. The adventitia of the arteries is swollen and infiltrated so as to show unusually clearly its fibrillar structure. The middle coat is also thickened (Fig. 1). In some places the arteries are quite obliterated.

Changes similar to those occurring in the skin occur to a less or equal extent in connective tissue everywhere, and, in a similar way, tend to crowd or

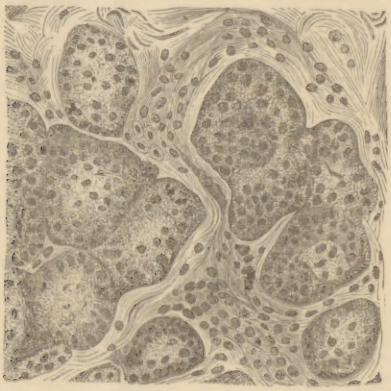

Fig. 2.—Section from the uvula showing glandular structure and intervening overgrowth of fibrillæ and nuclei. Magnified 200 diameters.

even destroy the essential elements of the part. The tongue is swollen, and its muscular and other elements in microscopical sections fall away from one another, separated by the overgrowth of cement. The changes are well seen in the uvula (Fig. 2), and probably exist in every part of the respiratory organs

and digestive apparatus. The heart, as a whole, is enlarged and firm, the left ventricle dilated and hypertrophied, its muscular elements being separated and even destroyed by the new material, while the great vessels at its base are atheromatous. The kidney is not enlarged or notably discolored, but it is too firm, and, while its surface is smooth and capsule not adherent, the cortical substance is atrophied and presents the aspect of granular kidney. In microscopical sections the very abundant transparent intertubular overgrowth is seen to compress the excretory structures, in part imitating the microscopical appearance of the early stage of granular kidney, the capsule of the Malpighian body in some instances being pressed in upon the contained glomerulous almost to the extent of obliterating the latter. The spleen and liver are also too firm, and in the latter a certain number of hepatic cells have atrophied under pressure. That from two-thirds to three-fourths of the thyroid gland are destroyed is regarded as an important matter by some, especially Dr. Hilton Fagge, to whose opinions it will be necessary to refer later.

In the first two cases, Dr. Ord could not satisfy himself that there existed the same or any parallel condition (excepting some degeneration of the arteries) in the central organs of the nervous system. Nevertheless, Drs. Goodhart, Hammond, and Hadden were fully persuaded some analogous lesion existed in these structures, and in Dr. Lloyd's case, the tissues of which are still being examined, Dr. Ord has found a general increase of the connective tissue of the cord, especially around the arteries and central canal; but he has not found any evidence of destruction or degeneration of the nerve-elements. In Dr. Lloyd's case, the dura mater was firmly adherent to the cranial bones. There was much atheroma in the vessels at the base of the brain. The cerebral convolutions were flattened, the right hemisphere especially being atrophied, while the ventricles were normal. The serous cavities contain more or less fluid, the chemical composition of which has not been compared with that of ordinary effusions.

Clinically, myxœdema is characterized by a "gen-

eral œdematous condition of the skin, unassociated with albuminuria, and combined with physical and mental torpidity." The patients are mostly stout adult women, who at first sight have the aspect of those suffering from renal disease. But the mucoid œdema, unlike ordinary œdema, does not gravitate on changing the patient's position, and the skin does not pit on pressure. Because the cutaneous glands are choked, there is no sebaceous secretion, and little or no perspiration, the skin being dry and, excepting that of the face, coarse, and sometimes scaly —much the same condition as that in which one's hands are after washing them in strong alkaline solutions. To the touch the skin loses its elasticity, becomes somewhat doughy with the soft solid infiltration of the subcutaneous tissue, and feels as dry and harsh as leather, or even emery paper. It is apt to become yellowish as the disease advances. That of the face has a dry but smooth, delicate, slightly translucent look, resembling wax or alabaster. This waxy appearance is very striking; the bloodless circle around the eye contrasts with the persistent, circumscribed, delicate rose tint of the cheek, readily increased in color by emotional influence, the two meeting abruptly at the lower border of the orbit. The broadened features and puffy cellular tissue around the eyes suggest but do not imply the existence of albuminuria. The lower eyelid is swollen in hanging folds, which do not yield to pressure. The nose is large, alæ nasi thickened, and the base flattened, so as to cause the eyes to appear too far apart. The somewhat cyanotic lips, thickened and pendulous, especially the lower, are separated by an expressionless, transverse slit, all the more slit-like because the mouth opens only a little by an up and down movement of the lips. In fact the whole face is placid or expressionless, as if in a mask.

The hair is fragile, and tends to fall off, perhaps to a greater extent (Charcot) from the pubes and axillæ than from the scalp. Dr. Sémon's case had lost the hair from every part. The tongue is thick and too large for the alveolar cavity, and is liable to be bitten, as it gets in the way of the teeth. Tooth-

less patients, for this reason, will not wear false teeth. The soft palate, inner surface of the cheeks, fauces, and pharynx are swollen. The larynx presents a glistening mucous surface and anæmic cords. This condition of the voice cavities, together with want of power in the muscles of articulation, interferes with natural speech. It becomes low-pitched, slow, uncertain, and measured ("scanned"), monotonous, and nasal, is frequently interrupted by an act of swallowing (done to displace the swollen uvula), and little explosive sounds produced in the posterior nares, in some respects resembling the voice of acute tonsillitis. Respiration may be more or less difficult, and some patients suffer from bronchitis.

The neck is full, and the skin and subcutaneous tissue may be thrown into permanent unyielding folds. In most cases it is difficult to detect the thyroid gland, partly because the neck is so thick, and partly because the gland is largely destroyed. Above the clavicle on either side is commonly a fatty tumor, similar to that found in sporadic cretinism. Dr. Hadden has seen a similar tumor flattened beneath the temporal muscle. The thickened hands lose their markings and contour, and become expressionless, the fingers pressing against one another so as to become square in section instead of round, giving to the whole hand the "spade-like" appearance of Dr. Gull. The fingers are flexed and extended with difficulty. The hands are very clumsy; it is troublesome, or impossible, to thread a needle. The nails, like the hair and teeth, are fragile and easily broken. The feet are similarly affected. Gloves and boots become too small. Walking is difficult and cannot be kept up for long, and may be attended with a sense of pressure in the lumbar region. The gait is a slow, deliberate shuffle, waddle, or stagger, with general quivering at each step, apparently an effort at balancing, as though the flexors and extensors could not act in harmony, and the quivering was set going to effect the adjustment. The quivering is not the trembling of spinal disease. The patients are subject to sudden falls when walking, caused by the flexors ceasing to act before the extensors begin,

letting the body fall between the two. Both ligamentæ patellæ have been ruptured in succession in one of Dr. Ord's cases by the violent tardy action of the extensors during a fall. Co-ordination is bad as to time, but there is no paralysis (nor numbness and tingling). There is want of tone, but no wasting of the muscles. Dr. Andrew Clark says in his cases the inco-ordination was worse in the dark or when the patient was blindfolded, resembling ataxy in this respect.

The inco-ordination Dr. Ord believes to be due to the partial insulation of the peripheral nerve-terminations in the skin and muscles; so, notwithstanding the skin is everywhere sensitive, perception is slow, and muscular response tardy. This slowness of perception and tardiness of response belong to all other acts of the patient as well as to that of walking. It contributes to the troubled speech and clumsiness of the hands. The simplest acts of life —dressing, knitting, and the like—require double, or more than double, the time usually necessary. In advanced cases this is very distressing; the day is spent in chasing the duties that should have been accomplished during the first hours of it. The slowness and clumsiness cause the patient to be timid, and she does not like to venture into the street alone. Not only is slow perception followed by slow action, it is also followed by slow thought. The mental act, though slow, is well done, however, and the patient is painfully aware of her general slowness, which she is unable to overcome. She may be somewhat morose and irritable. She can write; her memory, though in some cases impaired, is fairly good until late in the disease, when delirium, or even incurable insanity, may supervene. Then, too, the special senses may fail. Headache is sometimes pronounced. She gets in the way of being indifferent to all that goes on about her, and is inclined to sleep a good deal.

This general lethargic condition of the body and mind is worse in winter than in summer. Cold is keenly felt. This is not simply a subjective symptom; the color of the lips, already noted, and the

somewhat cyanotic extremities, and above all the actual axillary temperature tell too plainly its objective character. In a few notes I made at the bedside of one of Dr. Ord's cases, I found the axillary temperature ranged for some days between 96.4° F. and 97.8° F. Only in one instance has Dr. Hadden seen the temperature above normal, and then it was only 99.2° F. In all other instances the temperature has been below normal by one, two, or more degrees, with slight variations from day to day and from morning to night. The temperature is usually a little higher in one axilla than the other (Duckworth). In one of Dr. Ord's cases the temperature, several hours before death, was 87° F., and a few minutes before death only 79° F. The heart is weak, sometimes with, and sometimes without a murmur. The pulse is small and regular, varying in frequency between forty-five and eighty-five, being commonly below sixty. Toward the last the arteries became tortuous, their coats thickened, and the second sound at the base of the heart accentuated, as in cases of granular kidney. Indigestion and constipation are frequently present, as might be expected. The excretion of urea is much less than normal. In a number of cases in St. Thomas's Hospital the quantity of urea passed in twenty-four hours was reduced to from two-fifths to one-eighth its normal quantity, the reduction being in keeping with general sluggishness and low temperature. The quantity of urine is about normal, or a little less, and of low specific gravity, but contains no albumen, nor casts, until late in the disease. In women there is frequently more or less uterine trouble, but not sufficient to interfere with pregnancy and labor.

In addition to the œdema patients commonly have considerable subcutaneous fat. One thigh measured thirty-nine inches in circumference. They sometimes complain subjectively of "bands" binding down their muscles, constricting a limb perhaps. In eight or nine cases Dr. Duckworth has also noticed moles, acquired, not congenital, on the face, scalp, and shoulders. He suggests there may be a

relation between the mental torpor and the moles in myxœdema, similar to that existing between the mental condition and the cutaneous growths in molluscum fibrosum.

The prognosis of myxœdema is bad. Beginning insidiously, it very slowly and surely advances; the symptoms, perhaps scarcely noticeable at first, become gradually more marked, while others develop. Years—five, six, a dozen or more, perhaps—slip by in this way. Some day a noticeable change takes place. We have already had occasion to note some of the symptoms of the last stage. Renal trouble supervenes with its albuminuria and casts, ordinary anasarca, tortuous, thickened arteries, arterial tension, accentuated second sound of the heart, and hypertrophy of the left ventricle. Curiously, as these nephritic symptoms become established, there is for a short time improvement in the general condition. But to this last stage also belong the decided failing of memory, impairment of the special senses, delusions, more or less delirium, and even persistent alienation. Toward the last the skin tends to become wrinkled and movable on the parts below. The muscular and will-power may become so feeble as to allow the chin to fall against the sternum, producing marked dysphagia. In some cases the hanging head, the coarsely broadened features, the saliva dribbling from between the separated blubber lips, together with the general torpidity, both physical and mental, present indeed a very cretinoid aspect. Eventually, with a greatly reduced temperature, the patient becomes comatose and dies.

All treatment, hygienic, tonic, stimulant to the circulation, has failed to check the general progress of the disease. The effect of living in a warm climate or of wearing Dr. Chapman's spinal bags would seem worthy of a trial.

After the elucidation Dr. Ord has given myxœdema its differential diagnosis is not difficult. Though it has symptoms in common with cretinism, the facts that it begins in adults, well-developed physically and mentally, and is not endemic or in any way associated with goitre, at once distinguish it from both

sporadic and endemic cretinism. In the early stages it is easily distinguished from Bright's disease. The swollen skin does not pit on pressure, the urine is normal, or nearly normal, in quantity, and contains neither albumen nor casts. Myxœdema is now a definite disease, while polysarcia is a vague term and may mean nothing more than obesity. Sclerema and allied conditions differ in having a hard skin and in being local, with a tendency to heal in one direction as they extend in another. Ataxy seldom occurs in women, is not associated with mucous œdema, while paralytic and neuralgic symptoms are prominent.

In the first two post-mortem examinations Dr. Ord was unable to detect a lesion in the nervous centres. He was, therefore, led to regard the mucous swelling in other parts as the direct or indirect cause of all the symptoms. We have already seen how some of the symptoms evidently depend on this swelling. Before following out Dr. Ord's fuller explanation, it would be well to glance at Dr. Hilton Fagge's opinions* already referred to. From the cretinoid stand-point, the destruction of from two-thirds to three-fourths of the thyroid gland in myxœdema was somewhat in favor of his views. He and Mr. Curling had found no thyroid gland present in cases of sporadic cretinism in England, and as the worst cases of endemic cretins often had no bronchocele, he believed there was an antagonism between the thyroid gland and cretinism. When present the thyroid was a kind of filter, or safety reservoir, which by enlarging saved the patients from cretinism; they suffered with goitre instead. When the thyroid was absent, other causal conditions being present, cretinism resulted. He was inclined to believe myxœdema identical with the sporadic cretinism of children, seen in England, and due to the mucoid destruction of the thyroid gland. Most other observers, however, are opposed to this view of identity, and Dr. Ord, who at first entertained a somewhat cretinoid view of myxœdema, and

* Transactions Royal Medical and Chirurgical Society, 1871; Lancet, March 11, 1871; British Medical Journal, March 11, 1871.

hoped to investigate cretinism from a myxœdema stand-point, in places where cretinism is endemic, regards the question of overgrowth or atrophy of the thyroid as of little importance. Dr. Ord believed the padding of the nerve-terminations in the skin and in the muscles would account for the slowness of motion. Further, the padding made of the skin a more or less insulating cushion which interrupted a means of communication between the outer world and the nervous centres, upon which the education and development of the latter largely depend. In fact, Dr. Ord held that the natural process of development of the central nervous organs was directly dependent upon the exercise of these organs, stimulated to work by impulses from the periphery—that the surroundings of the growing animal "lick it into shape," so to speak. He also held that the intrusion of an insulating medium would tend to arrest development in proportion to the completeness of insulation. The intrusion of myxœdema, he thought, then, was a sufficient cause to give rise to the increasing torpor of the centres and the gradual mental impairment, the brain getting rusty, as it were, for want of proper exercise. He cited instances of temporary torpor produced by temporary failure of normal peripheral stimulation, and thought the long-continued influence of a slight failure could be expected to be followed by a gradually increasing torpor of the centres, just as any other unused part wastes for want of exercise.

Dr. Goodhart has objected to Dr. Ord's rationale. He admits the possibility of such an explanation were the disease one of infancy, but as it occurs in adults, when the brain has completed its development, he believes Dr. Ord's views untenable. He thinks past impressions would furnish mental food. Persons become blind without suffering any impairment of intelligence, and intelligence may be more active after than it was before the accident. One might add, too, the sense of touch is not lost in myxœdema; its only impairment is manifest in slow response. Now, a response at the periphery necessitates six acts, each of which involves a length of

time the physiologist can measure: 1, the peripheral impression; 2, the transmission to the brain; 3, the perception by the brain; 4, the determination to respond; 5, the transmission of the response; and 6, the peripheral act. Of the whole time required for the six acts by a person in health, the mental acts (3 and 4) have about one-fourth, and the peripheral impression (1) about one-tenth. To the slowness of which one or more of these acts the slowness of myxœdema is due can only be determined positively by experiment. Further, if one pad one's own fingers with various materials, one finds, if he makes through the padding an impression which can be felt at all, he can feel it as quickly, apparently, as he could were a thinner or no padding present—certainly there is no "perceptible" difference. It is possible, however, that the padding of myxœdema benumbs the touch-corpuscles by compression as well as by partial insulation. But aside from all this the mental symptoms seem to require a central as well as a peripheral lesion. Drs. Duckworth, Hammond, and Hadden have believed a lesion in the connective tissue of the nervous centres, analogous to that found in other parts, necessary to account for the nervous symptoms. This view has now been confirmed by a post-mortem examination, the result of which, so far as it has been obtained, was reported by Drs. Lloyd and Ord before the Clinical Society, January 14, 1881. At the same meeting the president, Dr. Greenhow, said, in one case within his experience, there was found distinct sclerosis of the spinal cord.

Dr. Hadden calls attention to the fact that myxœdema patients resemble cold-blooded animals in their torpid circulation, low temperature, and inactivity of physiological processes, suggesting the condition is due to a lesion of the sympathetic involving the vasomotors. Dr. Duckworth believes the disease has a trophic neurotic origin.

The facts Dr. Andrew Clark has collected are at present in the hands of Dr. Burnet for arrangement and publication, but he imagines the stages of the disease are marked by, 1, affections of the nervous

system; 2, renal inadequacy; and 3, affections of the circulatory system. We await with interest Dr. Clark's promised publication and the full report Drs. Ord and Savage are to make on the tissues of Dr. Lloyd's case.

Finally, then, until the results of farther investigations are known, we may consider myxœdema a substantive disease having a trophic neurotic origin, resulting in an increase of the mucin cementing material of connective tissue in all parts of the body; that its phenomena are due to the partial insulation, compression, or destruction of the more essential elements of structure in the various parts by this mucoid overgrowth of the connective tissue; and that the disease slowly but inevitably progresses to a fatal termination in spite of all treatment.

For the material of this paper I have been obliged to draw largely from articles Drs. Ord and Hadden were kind enough to give me while in London. I thank them for their kindness, and Mr. Seymour Taylor, of St. Thomas's Hospital, London, for his, to whom I am indebted for the sections of myxœdematous structures exhibited under the microscopes tonight.